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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,109	06/02/1999	KIM NASMYTH	0652.1880000	5712

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EXAMINER

LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 07/02/2002

20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/308,109

Applicant(s)

NASMYTH ET AL.

Examiner

Diana Johannsen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22,23,25 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22,23,25 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group II, claims 22, 23, and 25-29 and species human APC, APC-11, and yeast cell in Paper No. 19 is acknowledged. The traversal is on the ground(s) that: (1) "[A]s a search conducted for Group II would *necessarily* encompass the same subject matter as a search conducted for Group I, Applicants assert that the search for both groups would not be an undue burden, and therefore should be examined in the same application (see M. P. E.P § 803)."; (2) "searching for all species of the claims would not present an undue burden." since "a reasonable search for any APC subunit would encompass the remaining APC subunits." and "a reasonable search for either the yeast or human version of APC or expression of APC in either human or yeast cells would also overlap to a degree that searching".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that Groups I and II and all species will be examined together. First, a search conducted for Group II would not necessarily encompass the same subject matter as a search conducted for Group I. For example, the search required for Group II such as step (a) of claim 22 is not required for Group I since subunits of anaphase promoting complex can be made by known APC subunits. Second, searching for all species of the claims would present an undue burden on the examiner. For an example, polypeptide species in claim 14 are patentably distinct species and require different searches. Third, the examiner agreed with applicant that "a reasonable search for either the yeast or human version of APC or expression of APC in either human or yeast cells

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would also overlap to a degree that searching". However, these searches will not be coextensive.

For an example, a search for yeast APC will not use a keyword "human".

The requirement is still deemed proper and is therefore made FINAL.

2. This application contains claims 1-5, 14-21, and 24 drawn to an invention nonelected with traverse in Paper No. 19. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 22, 23, and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Since the specification does not have a definition of APC, this rejection based on the definition of APC defined by Jan-Michael Peter (Experimental Cell Biology, 248, 339-349, 199) wherein "[T]he APC is composed of more than 10 constitutive subunits and associates with additional regulatory factor in mitosis and during the G1 phase of the cell cycle." (See abstract).

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In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance on how to reconstitute a recombinant APC complex composed of more than 10 constitutive subunits. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether more than 10 recombinant individual subunits can work together to form a functional APC complex (E3 complex) in *in vitro* (Page *et al.*, Annual Review of Biochemistry, 68, 583-609, 1999). In page 586, second paragraph and page 604, first paragraph, Page *et al.*, stated that "[L]ittle, if anything, is known about how the individual APC subunits work together to form a functional E3 complex." and "the sheering number of subunit (at least eight essential subunits in budding yeast) required for cyclosome activity, not to mention specificity factors and activating kinase, will make the *in vitro* reconstitution of APC activity from purified components a daunting task."

Claims 22, 23, and 25-29 are directly to a method for identifying substances that inhibit rapidly proliferating cells by interfering with the cell's entry into the subsequent cell cycle by testing APC ability to ubiquitinate an APC substrate. The specification only describes that the

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expression systems such as baculovirus and the yeast *Pichia pastoris* offers the possibility to simultaneous expression several subunits to generate active complex (see page 6). However, the specification does not provide a guidance how to reach this goal. Applicant may argue that the expression systems such as baculovirus and the yeast *Pichia pastoris* are well established protein expression systems and a lot of different proteins have been produced by these systems, and one of skill in the art will have no problem to make APC using the similar methods. Although the examiner agreed with applicant in general concept, this is not the case here. First, the precise number of APC subunits is still not known (Peter, Experimental Cell Biology, 248, 339-349, 1999, see page 341, right column) and there is no predictability that the *in vitro* reconstitution of APC activity from purified components can form a functional APC complex. Second, the examiner could not found a successful report in reconstituting an APC complex composed of more than 10 constitutive subunits during prior art search (including applicant's papers). With these unpredictable factors, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes reconstitute a functional recombinant APC complex using more than 10 constitutive subunits.

5. Claims 22, 23, and 25-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assembling some APC subunits to form a functional APC, does not reasonably provide enablement for assembling any kind or/and any number of APC subunit (s) to form a functional APC. The specification does not enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Since the specification does not have a definition of APC, this rejection based on the examiner's definition of APC wherein APC is composed of at least one APC subunit.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance on how to reconstitute APC complex using any kind or/and any number of recombinant subunit(s). While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether any kind or/and any number of APC subunit(s) can work together to form a functional APC complex (E3 complex) in *in vitro*.

Claims 22, 23, and 25-29 are directly to a method for identifying substances that inhibit rapidly proliferating cells by interfering with the cell's entry into the subsequent cell cycle by testing APC ability to ubiquitinate an APC substrate. The specification only describes that the expression systems such as baculovirus and the yeast *Pichia pastoris* offers the possibility to

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simultaneous expression several subunits to generate active complex (see page 6). However, the specification does not provide a guidance to assemble any kind or/and any number of APC subunit(s) to form a functional APC. During prior art search (including applicant's papers), the examiner found a successful report in reconstituting a functional APC complex composed of CDC27 and CDC16 APC subunits (see US Patent No., 5,726, 025, filed on April 20, 1995). With these unpredictable factors, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes reconstitute a functional recombinant APC complex using any kind or/and any number of APC subunit(s).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22, 23, and 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 23 and 25-29 are dependent on claim 22.

8. Claim 22 is rejected as vague and indefinite in view of the phrase " cells from the budding yeast *Saccharomyces cerevisiae* or from human cells one or more endogenous genes encoding a known APC subunit" because it is unclear what it intended. Does this phrase mean that cells from the budding yeast *Saccharomyces cerevisiae* or from human cells contain one or more endogenous genes encoding a known APC subunit or mean something else? Please clarify.

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9. Claim 22 recites the limitation "said APC" in the claim. There is insufficient antecedent basis for this limitation in the claim since "subunits of Anaphase Promoting Complex (APC)" is different from "Anaphase Promoting Complex (APC)".

Response to Arguments

10. Applicant's arguments with respect to claims 11-13 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

12. No claim is allowed.

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13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
June 21, 2002



ETHAN C. WHISENANT
PRIMARY EXAMINER